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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,181	08/02/2006	Stefan Evers	21729	8450

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HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
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EXAMINER	
GITOMER, RALPH J	
ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,181	EVERS ET AL.	
	Examiner	Art Unit	
	Ralph Gitomer	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-23 and 27-37* is/are pending in the application.

4a) Of the above claim(s) *27-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The amendment received 11/29/07 has been entered and claims 21-23 are considered here. The amended title is acceptable.

It would appear the point of novelty is screening for PDE4D isotypes of PDE4 to find inhibitors that will treat atherosclerosis or restenosis. It was known to do the same with PDE4 which may have been a mixture of isotypes so a specific inhibitor for PDE4D only would be presumed to have greater treatment specificity.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of Frenette and Gretarsdottir.

Frenette (WO 00/64874) entitled "Heterosubstituted Pyridine Derivatives as PDE4 Inhibitors" teaches on page 2, the existence of multiple PDE4's raises the prospect of obtaining inhibitors that are selective for individual isoforms, thus increasing the specificity of action of such inhibitors. The cDNA's of each of A, B, C and D isoforms have been reported. Many of the PDE4 inhibitors which have been synthesized have lacked selectivity and are reported to emetic such as rolipram. On page 11 line 22 treating arterial restenosis and atherosclerosis is taught.

Gretarsdottir (US 2005/0287551 A1) entitled "Susceptibility Gene for Human Stroke; Methods of Treatment" teaches in paragraph 6 on page 1, there are at least 9 isoforms of PDE4D and the PDE4D gene is involved in the pathogenesis of stroke, possibly through atherosclerosis. On page 2 at the end of paragraph 7 predisposition to stroke or susceptibility to stroke can be assess by determining PDE4D isoform levels, preferably the level of expression of PDE4D7 and/or PDE4D9 is assessed. On page 2 paragraph 8 teaches an assay for identifying agents that alter the activity of one or more PDE4D polypeptides or isoforms. In paragraph 11 regulating isoform expression with pharmaceutical compositions is discussed.

The claims differ from Frenette in that they are directed to screening and identifying modulators of PDE4D.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to screen and identify modulators of PDE4D in view of the teachings of Frenette because Frenette teaches "obtaining" inhibitors for specific isoforms of PDE4 in order to avoid the problems with non-specific inhibitors of PDE4. And these inhibitors would be employed to treat arterial restenosis and atherosclerosis.

The claims differ from Gretarsdottir in that they include inhibiting restenosis.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to inhibit both atherosclerosis and restenosis in view of the teachings of Gretarsdottir because Gretarsdottir specifically teaches treating atherosclerosis and to then employ the same compounds to treat additional aspects of atherosclerosis such as restenosis would have a high expectation of success. In general, the same treatments for atherosclerosis are also employed for restenosis because the pathophysiology of the same tissue is closely related. And of course the reason the stenosis occurred in the first place was likely due to atherosclerosis so restenosis is also likely due to atherosclerosis.

Applicant's arguments filed 11/29/07 have been fully considered but they are not persuasive.

Applicants argue that Frenette does not disclose activity of PDE4 as related to atherosclerosis or stenosis. And Frenette does not disclose administering a compound suspected to be an activator or inhibitor of PDE4 to the PDE4 target. The teachings of Gretarsdottir first appear in the application filed April 18, 2003.

It is the examiner's position that Frenette teaches on page 11 line 22 PDE4 inhibitors are useful to treat arterial restenosis and atherosclerosis. The document shows a number of protocols and examples to determine the activity of inhibitors of PDE4, see page 40 for a screening assay where IC50 values are determined.

Regarding Gretarsdottir, the application 10/255,120, publication 2004/0091865 filed September 25, 2002 contains the teaches as described, see particularly paragraphs 7, 13 and 17 for example.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the following applies in all occurrences.

In claim 21 "the use of PDE4 as a target" lacks antecedent basis and does not specify how it is used for what sort of target.

This application contains claims 27-37 drawn to an invention nonelected with traverse in the reply filed on 5/22/07. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (571) 272-0916. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ralph Gitomer
Primary Examiner
Art Unit 1657